America's Blood Centers®
It's About Life.

725 15th Street NW Suite 700, Washington, DC 20005
Tel: 202-393-5725 Fax: 202-393-1282
1-888-USBLOOD www.AmericasBlood.org

Sent by E-mail
No paper sent

August 23, 2004

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: Docket No. 2004D-0193: Draft Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

Dear Docket Officer:

America's Blood Centers appreciates the opportunity to comment on the Food and Drug Administration's draft guidance on the eligibility of donors of tissues, cells and tissue-based products (HCT/Ps). We applaud FDA for taking a strong step toward assuring the safety of these products.

For your information, ABC is a national network of locally-controlled, not-for-profit community blood centers that collect almost half of the US blood supply from volunteer donors. Many ABC members are actively involved in the collection, processing, storage and distribution of HCT/Ps as well as blood and blood components.

Our specific comments on the draft guidance follow.

1. Section II, Paragraph 1-B *[Who Makes the Donor Eligibility Determination?]*

"A 'responsible person' must make the donor-eligibility determination (§ 1271.50(a)). A responsible person is one who is authorized to perform designated functions for which he or she is trained and qualified (§ 1271.3(t)). You are permitted to make the donor eligibility determination only if you are trained, qualified, and authorized to do so. The donor eligibility determination must be documented (§ 1271.50(a))."

Comments: Since the terms "trained, qualified, and authorized" are not clearly defined, this means that for some tissue donors, physician designees (non-physicians) could be permitted to make final donor eligibility determinations. The American Association of Tissue Banks (AATB) Standard F1.100 (Donor Suitability Review) states that, "Although the donor's medical, social, and sexual history may be preliminarily screened by technical staff to evaluate acceptability for retrieval or processing, cells and/or tissue shall not be released for transplantation without final review of donor suitability by the Medical Director or licensed physician designee." AATB Standards also require that the Medical Director be a licensed physician. ABC agrees with AATB's standards in this area.

ABC Recommendation: FDA should revise this section to require that the suitability decision be made by a licensed physician

2. Section III. Donor Screening. [*Physical Examination of Living Donors]*

Part C: "The purpose of the physical assessment of a cadaveric donor or the physical examination of a living donor, is to assess for physical signs of a relevant communicable disease and for signs suggestive of any risk factor for such a disease…. Since this is a step in determining donor eligibility, FDA recommends that you establish and maintain standard operating procedures (SOPs) for the conduct of the physical assessment or physical examination (§ 1271.47)." Part G: "Relevant medical records include the report of the physical assessment of a cadaveric donor or the physical examination of a living donor (§1271.3(s)). FDA recommends that you review those records for any of the following signs that may indicate high-risk behavior for or infection with a relevant communicable disease. Some of the following are not physical evidence of HIV, hepatitis, syphilis, or vaccinia but rather are indications of high-risk behavior associated with these diseases. [The draft guidance then lists 14 examples of physical evidence to look for when examining a living donor, including]: "physical evidence for risk of sexually transmitted diseases such as genital ulcerative disease, herpes simplex, syphilis, chancroid; "for a male donor, physical evidence of anal intercourse including perianal condyloma; oral thrust; corneal scarring consistent with vaccinial keratis."

Comment: The requirement for physical assessment of a cadaveric donor is an appropriate one focused on assuring that information provided by the family is not contradicted by observable facts. For volunteer, uncompensated living donors, screening questionnaires provide a reliable assessment of the donor's history. . Mothers delivering babies will also have been examined before the collection of cord blood. All living donors (including stem cell donors) may be queried in detail about risk factors and health conditions. To require a specific physical examination of a living donor, particularly for evidence of sexually transmitted diseases, is duplicative, and extremely intrusive. This requirement could lead to a significant reduction of organ, cord blood, and hematopoietic stem cell donors.

ABC Recommendation: Delete the requirement for a specific physical examination for living donors. Screening by a donor medical history interview and infectious disease testing using assays currently licensed for blood donor screening are more than adequate, as clearly documented in the blood transfusion literature.

3. Section III. E. 9 Donor Screening. [*Close Contact with Hepatitis Patient]*

"FDA believes that the following conditions and behaviors increase the donor's relevant communicable disease risk. Except as noted in this section, we recommend that you determine to be ineligible any potential donor who exhibits one or more of the following conditions or behaviors. . . "persons who have had close contact within 12 months preceding donation with another person having clinically active viral hepatitis (e.g., living in the same household, where sharing of kitchen and bathroom facilities occurs regularly)

Comment: The requirement for deferring "close contacts" is unnecessarily broad. The American Association of Blood Banks (AABB) *Standards* for blood donor acceptability limit the definition of "close contact" for viral hepatitis to sexual (intimate) contact only. The draft tissue donor eligibility guidance already includes the requirement for deferral of potential donors with sexual contact with an individual at risk for HIV or HCV. In addition, in Section III.E.20, this draft defines "close contact" for a xenotransplantation product recipient as sexual contact or exposure "to blood, saliva, or other body fluids from the xenotransplantation product recipient (*e.g.*, through deep kissing, shared toothbrushes, razors, or needles, or through open wounds or sores)."

ABC recommendation: Revise the definition of "close contact" to sexual (intimate) contact.

4. Section III.E.16 *[Headache with Fever]*

". . . FDA believes that the following conditions and behaviors increase the donor's relevant communicable disease risk. Except as noted in this section, we recommend that you determine to be ineligible any potential donor who exhibits one or more of the following conditions or behaviors.... 16. persons who have had both a fever and a headache (simultaneously) during the 7 days before donation, we recommend that: The donor be deferred from donation; or The donor be deferred for 28 days after the interview for living donors who may donate at a later date.

Comment: We believe that this exclusion has the potential to exclude certain cadaver donors unnecessarily (*e.g.* donors with subarachnoid hemorrhages; motor vehicle accident victims cared for in the hospital for 7 days prior to death, etc.). We note that fever with simultaneous headache are listed in Section E as a separate risk factor for relevant communicable diseases; yet in section F.5 (F. What clinical evidence do I look for when screening a donor? WNV infection) fever and headache are listed as clinical evidence for West Nile Virus infection. Section F.5 also states that because signs and symptoms of WNV can be nonspecific, the clinical signs and symptoms must be considered in light of other information obtained about the donor.

ABC Recommendation: We recommend deleting section III.E.16. Should this be unacceptable, the section should be revised to state that this deferral recommendation is to be applied when evaluating a potential donor who is at risk for having been exposed to WNV and when no WNV testing will be performed. On its own, headache with fever should not require donor deferral.

5. Section 3.E 20.a and b [Excerpted] [Xenotransplant Recipients]

a. FDA recommends that you use the following xenotransplantation definitions: i. Xenotransplantation is any procedure that involves the transplantation, implantation, or infusion into a human recipient of either: (1) live cells, tissues, or organs from a nonhuman animal source; or (2) human body fluids, cells, tissues, or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs. . . . . b. To determine whether a potential donor has received a xenotransplantation product, or is the intimate contact of a person who has received a xenotransplantation product, we recommend that you ask if the potential donor, his/her sexual partner, or any member of his/her household has ever had a transplant or other medical procedure that involved being exposed to live cells, tissues, or organs from an animal. If the xenotransplantation product recipient is the potential donor or his/her sexual partner, FDA recommends that you defer the donor. If the recipient is a member of the potential donor's household, we recommend that you determine whether the potential donor has been exposed to blood, saliva, or other body fluids from the xenotransplantation product recipient (e.g., through deep kissing, shared toothbrushes, razors, or needles, or through open wounds or sores). If any of these are the case, FDA recommends that you defer the donor.

Comment: We accept the necessity to defer recipients of xenotransplants but believe that transplant programs should have primary responsibility to initiate this process as part of the xenotransplantation consent process. We also believe that transplant programs should educate the transplant product recipient about the risks of xenotransplantation, and this education should include information advising them that they should not donate blood or HCT/Ps.

We do not believe that deferral of intimate contacts of xenotransplants is justified. The inclusion of immune-intact donor contacts in the deferral group raises the concern that the next wave of deferrals will apply to those with extensive animal contact outside the limited setting of xenotransplantation—such as farmers, veterinarians, and abattoir workers. Our approach is based on two factors: (1) xenotransplantation recipients will be deferred under any circumstances—based on their underlying disease and administration of immunosuppressive drugs, and (2) deferral of intimate contacts, who

are not immunosuppressed, is excessively conservative at best, and at worst is a precedent that may lead to considering deferral of many others with repeated animal contacts outside the context of xenotransplantation, absent demonstrable risk to either donors or blood recipients.

ABC recommendation: Delete all recommendations for deferring contacts of xenotransplant recipients in this guidance.

6. Section 4.E. When do I collect a specimen for testing?

"You must collect the donor specimen for testing at the same time as cells or tissue are recovered from the donor, or, if this is not feasible, within seven days before or after the recovery of cells and tissue (§ 1271.80(b)).

Comment: A pre-mortem sample drawn within the defined time limits is preferable due to improved sample quality, and the affects of plasma dilution can be reduced or eliminated by locating a suitable ante-mortem blood sample (less dilute, or undiluted). The current wording can be interpreted as restricting the bank's choice to use the best blood sample available.

ABC Recommendation: We recommend deletion of the phrase "if this is not feasible".

7. Section V. *[CMV Testing]*

". . . "You must test donors of viable, leukocyte-rich cells or tissue for the following diseases, in addition to those listed in section V.A. (§ 1271.85(b)). You must use an FDA licensed, cleared, or approved test where such a test is available (§ 1271.80(c))." . . . We recommend that you use the tests listed in parentheses: b. Cytomegalovirus (FDA-cleared screening test for anti-CMV). Special note on CMV: CMV is not a relevant communicable disease or disease agent. However, establishments are required to test donors of viable, leukocyte-rich cells or tissues for CMV. A donor who tests reactive for CMV is not necessarily ineligible to donate HCT/Ps. You must establish and maintain an SOP governing the release of HCT/Ps from donors whose specimens test reactive for CMV (§ 1271.85(b)(2)). We recommend that the SOPs be based on current information on the potential for disease transmission from the type of HCT/P to be made available for use and that the SOP limit use of an HCT/P based on the CMV reactive status of the recipient."

Comment: Cord blood units listed on NMDP registry currently are tested for anti-CMV with results made available to the transplanting physician. For blood and blood components and organs, the decision about whether or not to transfuse/transplant a CMV positive unit to a CMV negative recipient is made by the patient's physicians. We believe that for cord blood and hematopoietic stem cells as well, the transplanting physician should determine whether a unit reactive for anti-CMV is appropriate for his/her patient.

ABC Recommendation: FDA should replace the requirement for the blood center to develop SOPs about the use of an HCT/P based on the CMV reactive status of the recipient with the following: "We recommend that the SOPs require notifying the attending physician of the CMV status of the donor. It is the responsibility of the potential recipient's attending physician to determine the recipient's CMV-reactive status and to determine whether the potential risks of CMV transmission are acceptable."

Yours truly,

Celso Bianco

Celso Bianco, MD

Executive Vice President